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Late Breaking Abstract Session
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1 - Late Breaking Abstract
Phase III randomized trial of laparoscopic or robotic versus abdominal radical hysterectomy in patients with early-stage cervical cancer: LACC Trial
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Objective: Minimally invasive radical hysterectomy is routinely performed in the management of patients with early-stage cervical cancer. The goal of this study was to investigate whether disease-free survival (DFS) among patients who underwent laparoscopic or robotic (MIS) was non-inferior compared to standard-of-care open (TARH) radical hysterectomy.

Method: This was a prospective randomized, international, multicenter, non-inferiority phase III trial, confirmed stage IA1 (lymphvascular invasion) to IB1 tumor. Histologic subtypes were squamous cell carcinoma, adenocarcinoma, or adenosquamous carcinoma. Randomization (1:1). Aimed to recruit 740 patients (370 per arm) to have over 90% power to declare non-inferiority in DFS at 4.5 years, with a margin of 7.2% (90% in TARH to 82.8% in MIS).

Results: At closure, 312 patients were randomized to TARH; 319 patients to MIS (83% laparoscopy and 16% robotic surgery). The majority (92% in both) were stage IB1. Treatment arms were well balanced on baseline characteristics, including age (mean 46 years in both) and BMI (median 26 vs 27 kg/m^2). In the TARH group, 88% received their randomized treatment versus 91% in the MIS group. Conversion rate to laparotomy was 3%. Table 1 shows the similarity of treatment groups on histopathology and adjuvant therapy. At the time of analysis, the information available at 4.5 years was 60%, with over 80% power for the primary endpoint and median follow-up of 2.5 years. The non-inferiority boundary of −7.2% for DFS at 4.5 years was breached (TARH 97% versus MIS 86%, difference −10.6%, 95% CI −16.4% to −4.7%, P = 0.87). MIS was found to have over a 3-fold increase in DFS events (7/312 vs 27/319, HR = 3.74, 95% CI 1.63–8.58, P = 0.002), which was consistent when adjusted for age, BMI, stage of disease, LVSI, lymph node involvement, and ECOG status. MIS was also associated with a decrease in overall survival (3/312 vs 19/319, HR = 6.00, 95% CI 1.48–20.3, P = 0.004). There were no differences in rates of intraoperative complications by treatment received (11% in both, P = 0.76).

Conclusion: In this prospective randomized trial, laparoscopic or robotic radical hysterectomy was associated with higher recurrence rates and worse overall survival when compared with the open approach in women with early-stage cervical cancer.

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2 – Late Breaking Abstract
Comparative effectiveness of minimally-invasive staging surgery in women with early-stage cervical cancer
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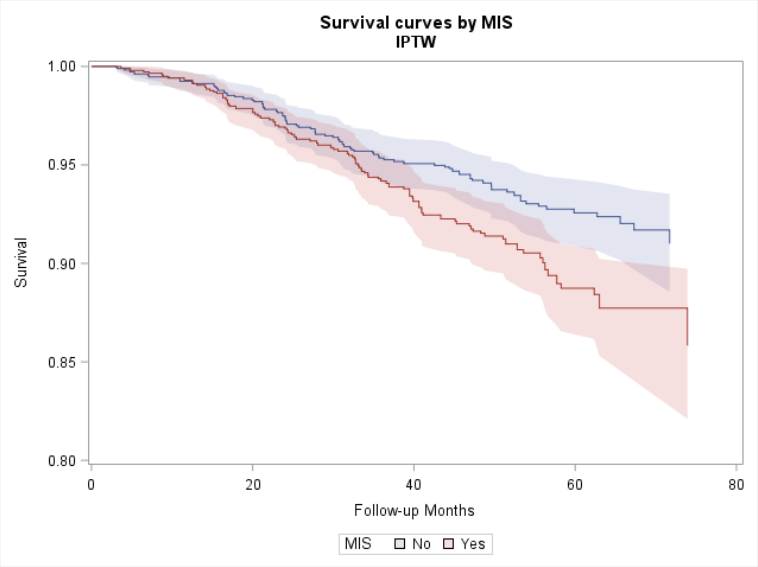
Objective: Despite the absence of randomized controlled trials, minimally invasive (MIS) radical hysterectomy (RH) is a widely accepted treatment for early-stage cervical cancer (CeCa). The aim of this study was to examine the association between use of MIS and survival among women undergoing RH for CeCa in a large U.S. population.

Method: We utilized the National Cancer Data Base to identify women diagnosed with stage 1A2–1B1 CeCa who underwent RH between 2010 and 2012. We used propensity score inverse probability treatment weighting (IPTW) to compare women who underwent RH by MIS or laparotomy but were otherwise balanced on covariates. Survival analyses utilized IPTW Kaplan-

Meier and Cox proportional hazard models. To assess whether these findings were due to causal effects, we conducted an interrupted time series to evaluate whether adoption of MIS led to a change in survival.

Results: We identified 1,166 (52.5%) women who underwent an RH via laparotomy, and 1,055 had MIS (47.5%). In the MIS group, 833 (79%) had robotic surgery. Patients who received MIS were more often white, were privately insured, were from zip codes with higher income and educational levels, were treated in academic centers, had smaller, lower grade tumors, and more often had adenocarcinomas. All covariates were well-balanced in the propensity-matched cohorts. There was no difference between the groups in rates of parametrial invasion (12% vs 9%, *P* = 0.09), positive margins (5% vs 5%, *P* = 0.47), or lymph node involvement (11% vs 9%, *P* = 0.15). The median follow-up was 51 months for MIS and 53 for laparotomy. Women who had MIS had 48% higher hazard of death from any cause compared to those who had laparotomy (HR = 1.48, 95% CI 1.10–1.98). In an interrupted time series, before adoption of MIS (2000–2006) there was a nonsignificant trend toward improved survival over time (annual percentage change 0.4, 95% CI 0.1–0.8). Adoption of MIS was associated with a significant change of trend (*P* = 0.02), with 4-year survival declining by 1.0% per year (95% CI 0.3–1.6) after 2006. See Figures 1A and 1B.

Conclusion: Despite minimal evidence of the benefits of MIS, a significant number of women with CeCa undergo MIS RH. Compared with laparotomy, MIS is associated with lower survival for women with early-stage CeCa.



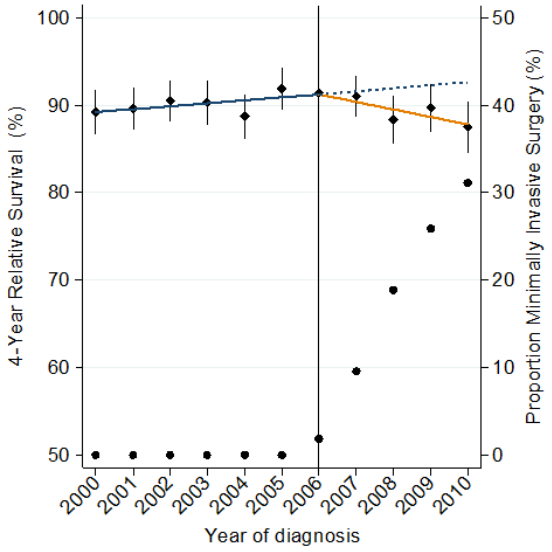


Fig. 1a. Kaplan–Meier survival curves for the propensity-matched IPTW groups. Women who underwent MIS RH had inferior overall survival compared with those who underwent laparotomy (plog rank = 0.02). The probability of death within 4-years of diagnosis was 8.4% among MIS compared with 4.7% among those who had laparotomy.

Fig. 1b. Interrupted time series evaluating the effect of adoption of MIS RH on 4-year relative survival among women with CeCa. The 4-year survival among women receiving RH for CeCa (diamonds) and 95% CI (whiskers) are plotted annually 2000-2010. The proportion of RH undertaken using a MIS approach (circles) is plotted on the right axis. In the years before the adoption of MIS there was a nonsignificant trend toward improved survival (annual percent change [APC] 0.4; 95%CI -0.1 to +0.8). Adoption of MIS was associated with a significant change of temporal trend (p=0.02), with 4-year survival declining by 1.0% (95%CI 0.3-1.6) per year annually after 2006.

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3 – Late Breaking Abstract

Topacio: Preliminary activity and safety in patients (pts) with platinum-resistant ovarian cancer (PROC) in a phase 1/2 study of niraparib in combination with pembrolizumab

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Objective: Patients with platinum-resistant ovarian cancer (PROC) have limited treatment options; objective response rates (ORRs) are 4%–16% for single-agent poly(ADP-ribose) polymerase (PARP) inhibitors in *BRCA* wildtype patients and 11%–15% for anti–PD-1 agents in pretreated OC patients. Inhibition of PARP in tumors treated with anti–PD-1 therapy may enhance immune response via generation of cytosolic DNA, which activates T cells via the stimulator of interferon genes pathway. Topacio is a phase 1/2 study evaluating the safety and efficacy of combination treatment with the PARP inhibitor niraparib and pembrolizumab in patients with triple-negative breast cancer or PROC. In the phase 1 portion, 9 OC patients were treated, of which 5 had a complete or partial response and 4 achieved stable disease (SD); 3 responders had tumors that were *BRCA*wt. Enrollment in the phase 2 OC cohort was completed September 2017; results are presented here.

Method: Patients in phase 2 of the study receive the recommended phase 2 dose of niraparib 200 mg orally once daily and pembrolizumab 200 mg intravenously on day 1 of each 21-day cycle. The niraparib dose may be escalated to 300 mg after the first 2 cycles if no hematologic toxicities are observed. Primary objective is to estimate the clinical activity of the combination treatment using ORR and a 2-stage design targeting ≈48 evaluable OC patients.

Results: As of the August 2017 data cutoff, 36 patients with OC had enrolled in phase 2: 29 had undergone ≥1 on-study scan and 13 had ≥2 scans. Median age is 60 years, with a median of 3 prior lines of therapy. Six patients had a partial response, 12 had SD, and 11 had progressive disease. Of the 6 patients with partial response, 5 remain on treatment, 3 (50%) were *BRCA*wt, and 2 of the *BRCA*wt patients were also PD-L1 negative. Treatment-related grade ≥3 events occurred in 16 patients (44%), the most common of which were anemia (16.7%), fatigue (5.6%), decreased platelet count (5.6%), and thrombocytopenia (2.8%). Updated efficacy, safety, and biomarker status data for OC patients enrolled in phases 1 and 2 will be presented.

Conclusion: Preliminary efficacy of niraparib and pembrolizumab combination therapy in heavily pretreated patients with PROC was shown, including those with *BRCA*wt and/or PD-L1–negative disease. No new safety signals were identified.

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4 – Late Breaking Abstract

An open-label, phase II basket study of olaparib and durvalumab (MEDIOLA): Results in germline *BRCA*-mutated (*gBRCA*m) platinum-sensitive relapsed (PSR) ovarian cancer (OC)

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Objective: Olaparib (Lynparza™) is a poly(ADP-ribose) polymerase inhibitor (PARPi) approved for the treatment and maintenance therapy of ovarian cancer (OC). Here, the objective was to assess the efficacy and safety of olaparib in combination with durvalumab (Imfinzi™), an antiprogrammed cell death ligand-1 (PD-L1) agent, in the platinum-sensitive relapsed (PSR) OC treatment setting (NCT02734004).

Method: Women with g*BRCA*m PSR OC with ≥1 prior platinum therapy were eligible. Patients received olaparib 300 mg (tablet) PO BID for a 4-week run-in, followed by a combination of olaparib 300 mg PO BID and durvalumab 1.5 g IV q 4 weeks, which was continued until progressive disease (PD). Tumor assessments were done at baseline, 4 weeks and every 8 weeks thereafter. The primary endpoints were disease control rate (DCR) at 12 weeks, safety, and tolerability. The secondary endpoints were DCR at 28 weeks, objective response rate (ORR), duration of response, progression-free survival (PFS), and overall survival. Biomarker endpoints included PD-L1 expression and evaluation of tumor-infiltrating lymphocytes. Olaparib previously showed a median PFS of 11 months in the OC maintenance setting, and addition of durvalumab was predicted to increase it to 18.3 months, corresponding to a DCR of approximately 90% at 12 weeks. The required number of patients to evaluate the endpoints was 31 patients, and 32 patients were enrolled.

Results: Median age was 59 years (range 44–76 years); 22 and 10 patients had g*BRCA1* and g*BRCA2* mutations, respectively. Median number of prior chemotherapy lines was 2 (range 1–6). The most common gr ≥3 adverse events were anemia (9%), increased lipase (9%), increased amylase (6%), and neutropenia (3%). Final interim look showed an observed DCR at 12 weeks of 81%, which was in the efficacy region. Six (19%) complete responses (CR) and 14 (44%) partial responses were

seen, resulting in an ORR of 63%. In patients with 1–2 prior chemotherapies (*n* = 22), the ORR was 68%, including all 6 patients with CR. Updated results for efficacy, safety, biomarker, and PK data will be presented. See Figure 1.

Conclusion: The combination of olaparib and durvalumab was well tolerated. Tumor responses in this initial analysis were higher compared to those reported for PARPi monotherapy. Enhanced responses were seen in patients with 1–2 prior chemotherapies. This nonchemotherapy combination may provide an efficacious and well-tolerated treatment option for g*BRCA*m PSR OC.

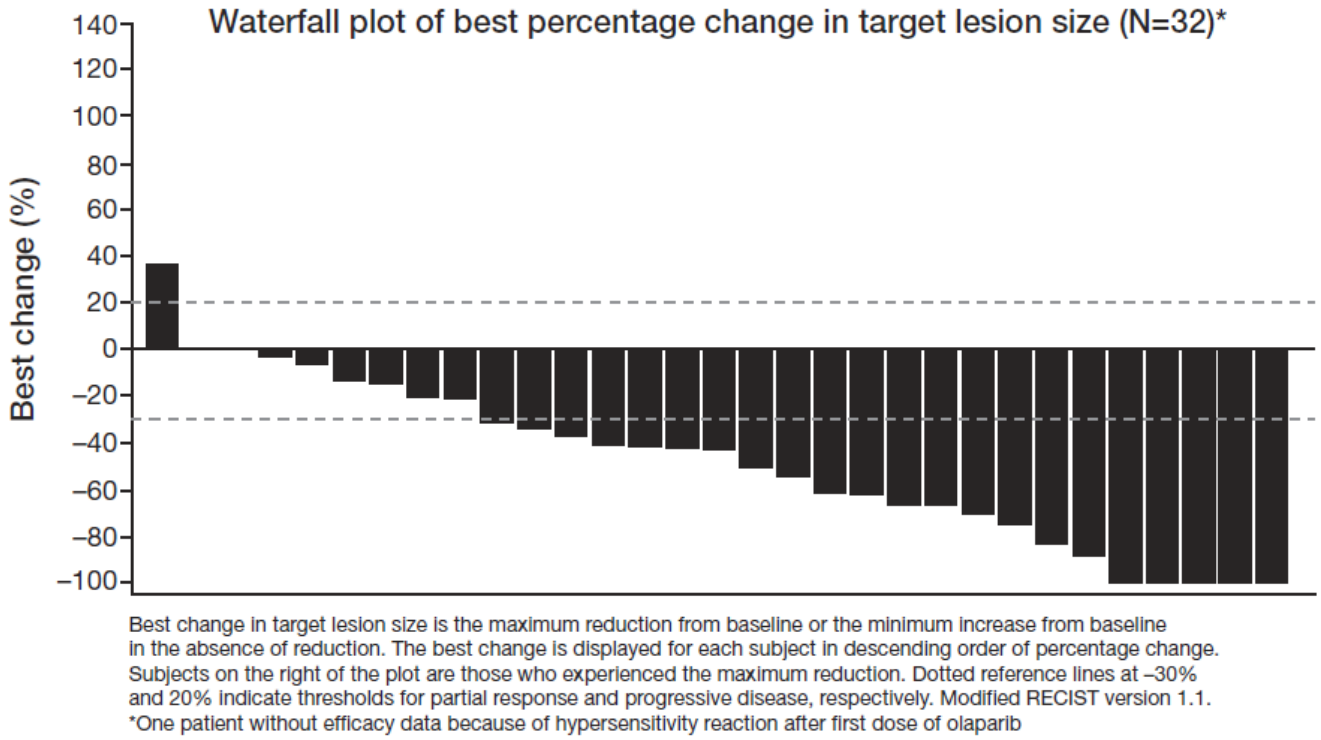

Fig. 1.